

What is claimed is:

1. An isolated population of cells comprising an expressible nucleic acid encoding proinsulin containing a proinsulin cleavage site and a glucose-regulated expressible nucleic acid encoding a protease capable of cleaving said proinsulin cleavage site to produce insulin.

2. The isolated population of claim 1, wherein said protease is furin.

3. The isolated population of claim 1, wherein said glucose-regulated expressible nucleic acid further comprises a transforming growth factor- α (TGF- α) regulatory element.

4. The isolated population of claim 1, wherein said proinsulin and said glucose-regulated protease are expressed from a single vector.

5. The isolated population of claim 4, wherein said vector is a retroviral vector.

6. The isolated population of claim 4, wherein said vector further comprises a selectable marker.

7. The isolated population of claim 1, wherein said cells express a hexosamine biosynthetic pathway enzyme.

8. The isolated population of claim 7, wherein said hexosamine synthetic pathway enzyme is glutamine:fructose-6-phosphate amidotransferase.

9. The isolated population of claim 1, wherein said cells are smooth muscle cells.

10. The isolated population of claim 1, wherein said proinsulin cleavage site further comprises
5 the following tetrabasic sequence comprising the amino acids:

Arg-Xaa-Lys/Arg/Xaa-Arg (SEQ ID NO:7),

wherein Xaa comprises any amino acid.

11. A three-gene vector comprising an
10 expressible nucleic acid encoding proinsulin containing a proinsulin cleavage site, a glucose-regulated expressible nucleic acid encoding a protease capable of cleaving said proinsulin cleavage site to produce insulin, and a selectable marker.

15 12. The three-gene vector of claim 11, wherein said protease is furin.

13. The three-gene vector of claim 11, wherein said glucose-regulated expressible nucleic acid further
20 comprises a TGF- α regulatory element.

14. The three-gene vector of claim 11, wherein said selectable marker is neomycin phosphotransferase.

15. The three-gene vector of claim 11, wherein said proinsulin cleavage site further comprises a
25 tetrabasic sequence comprising the amino acids:

Arg-Xaa-Lys/Arg/Xaa-Arg (SEQ ID NO:7)

16. The three-gene vector of claim 11 wherein said vector is a retroviral vector.

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5 17. A method of treating or preventing diabetes comprising implanting into an individual cells coexpressing proinsulin containing a proinsulin cleavage site and a glucose-regulated protease capable of cleaving said proinsulin cleavage site to produce insulin.

18. The method of claim 17, wherein said protease is furin.

10 19. The method of claim 17, wherein said glucose-regulated protease is encoded by a glucose-regulated expressible nucleic acid further comprising a TGF- α regulatory element.

15 20. The method of claim 17, wherein said cells are implanted in prosthetic grafts.

21. The method of claim 20, wherein said prosthetic graft comprises polytetrafluoroethylene.

20 22. The method of claim 17, wherein said proinsulin and said protease are expressed from a single vector.

23. The method of claim 22, wherein said vector is a retroviral vector.

24. The method of claim 22, wherein said vector further comprises a selectable marker.

25. The method of claim 17, wherein said cells are administered in a pharmaceutically acceptable carrier.

26. The method of claim 17, wherein said cells
5 are smooth muscle cells.

27. The method of claim 17, wherein said proinsulin cleavage site further comprises a tetrabasic sequence comprising the amino acids:

Arg-Xaa1-Lys/Arg/Xaa2-Arg (SEQ ID NO:7)

10 wherein Xaa1 and Xaa2 is any amino acid.

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28. A method of treating or preventing diabetes comprising implanting into an individual cells coexpressing proinsulin containing a proinsulin cleavage
15 site, a glucose-regulated protease capable of cleaving said proinsulin cleavage site to produce insulin, and a hexosamine biosynthetic pathway enzyme.

29. The method of claim 28, wherein said protease is furin.

20 30. The method of claim 28, wherein said glucose-regulated protease is encoded by a glucose-regulated expressible nucleic acid further comprising a TGF- α regulatory element.

31. The method of claim 28, wherein said
25 hexosamine biosynthetic pathway enzyme is glutamine:fructose-6-phosphate amidotransferase.

32. The method of claim 28, wherein said proinsulin and said glucose-regulated protease are expressed from a first vector and said hexosamine synthetic pathway enzyme is expressed from a second
5 vector.

33. The method of claim 32, wherein said first and second vectors are retroviral vectors.

34. The method of claim 32, wherein said first and second vector further comprises a selectable marker.

10 35. The method of claim 28, wherein said cells are implanted in prosthetic grafts.

36. The method of claim 35, wherein said prosthetic graft comprises polytetrafluoroethylene.

15 37. The method of claim 28, wherein said cells are administered in a pharmaceutically acceptable carrier.

38. The method of claim 28, wherein said cells are smooth muscle cells.

20 39. The method of claim 28, wherein said proinsulin cleavage site further comprises a tetrabasic sequence comprising the amino acids:

Arg-Xaa1-Lys/Arg/Xaa2-Arg (SEQ ID NO:7),

wherein Xaa1 and Xaa2 comprises any amino acid.

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